

IT IS CLAIMED:

1. A method for manufacturing an array of biomolecules that have complementary binding species, comprising:
 - 5 forming on a first substrate, a master-species array composed of a plurality of different species attached to selected regions on the first substrate, bringing a mixture of the biomolecules complementary to said species into contact with the master species array, such that biomolecules in the mixture bind with complementary species in the master array,
 - 10 positioning a second substrate into a confronting relationship with the master array, such that biomolecules bound to the master-species array are in proximate confronting relationship to corresponding array regions in the second substrate, and
 - transferring the biomolecules from the first substrate to confronting array regions in the second substrate, thereby to form an array of biomolecules on the second substrate.
2. The method of claim 1, wherein said biomolecules include a binding moiety selected from sulfhydryl or thiol, effective to react with and bind to the surface of the second substrate, when contacted with the second substrate during said transferring step.
- 20 3. The method of claim 2, wherein said biomolecules include a sulfhydryl binding moiety, and the confronting surface of the second substrate includes a gold film.
- 25 4. The method of claim 1, wherein said biomolecules are charged at a selected pH, and said positioning includes placing between confronting surfaces of the first and second substrates, a film of electrolyte solution at the selected pH, and said transferring includes applying across the first and second substrates, an electric field whose polarity and field strength are sufficient to cause the biomolecules bound to the first substrate to migrate to corresponding array regions of the second substrate.

5 5. The method of claim 1, for use in forming an array of different-sequence oligo- or polynucleotides, wherein said species include different-sequence oligonucleotides, and said biomolecules include oligo- or polynucleotides containing at least a segment that is complementary to one of said species.

10 6. The method of claim 5, wherein said oligo- or polynucleotide biomolecules include a binding moiety selected from sulfhydryl or thiol, and the confronting surface of the second substrate includes a gold film to which the moiety can bind.

15 7. The method of claim 5, wherein said second substrate is coated with an oligonucleotide having a given sequence to derivatize the surface of said second substrate, and each of the biomolecules bound to the first substrate has a segment whose sequence is common to the other biomolecules and complementary to the oligonucleotide coating the second substrate.

20 8. The method of claim 1, which further includes repeating the said bringing, positioning, and transferring steps multiple times, thereby to produce multiple arrays.

25 9. The method of claim 8, wherein the substrate of said master-species array is in the form of a cylindrical drum and the substrate of said complementary species arrays is in the form of a continuous roll of film

 10. The method of claim 1, applied to a master-species array that has itself been formed by the method of claim 1, to produce a subsequent generation of complementary replica arrays.

30 11. The method of claim 1, in which at least one of the processes is done on a roll-to-roll basis with at least one of the substrates being unrolled from a feed roller and re-rolled onto a take-up roller.

12. A sensor array device comprising:

a plurality of individually addressable deformable membrane elements having resonant frequencies that change when mass is added to or removed from the membrane in each sensor,

5 a readout system that detects changes in the resonant frequency of at least one membrane element in the array, and

a signal-processing system for determining, from detected changes in resonance frequency, the presence of a change in mass of said system.

10 13. A sensor array device for use in detecting the binding of analyte molecules to one or more array probes, comprising:

a substrate,

an array of vibratory elements formed on said substrate, each element having a vibratory membrane having with a characteristic resonance frequency,

15 when activated by an oscillating electrical field applied to the membrane,

a molecular species probe attached to the membrane of each element array, wherein binding of analyte molecules to a probe is effective to alter the resonance frequency of the associated membrane,

20 associated with each element, a pair of electrodes by which an electrical field can be applied across the element membrane,

a voltage source operatively connected to said electrodes for applying an oscillatory electric field to a selected element membrane, thereby to induce vibration in the membrane, and

25 a detector for detecting the frequency or amplitude of induced vibration in an element membrane, thereby to determine the presence or absence of analyte bound to each of one or more membranes in the device.

14. The device of claim 13, wherein the array includes a plurality of rows and plurality of columns of elements, and the pairs of electrodes associated
30 with the elements are formed by a plurality of row electrodes positioned on one face of a plurality of rows of elements, and a plurality of column electrodes positioned on the opposite face of a plurality of columns of elements.

15. The device of claim 14, wherein the voltage source is operable to excite selected row and selected column electrodes, thus to induce vibration in one or more selected elements.

5 16. The device of claim 13, wherein the voltage source is operable to apply a variable-frequency alternating electrical field across a selected element membrane, and said detector is operable to detect the frequency at which resonance occurs.

10 17. The device of claim 13, for use in detecting the presence or absence of each of a plurality of different DNA analytes, wherein said probes are different-sequence nucleic acid probes.

15 18. The device of claim 13, for use in detecting the presence or absence of each of a plurality of different polypeptide analytes, wherein said probes are different-polypeptide-binding probes.

19. An optically-addressed hybridization array sensor comprising:
an array of vibratory elements having a substantially rigid cavity covered
20 by a flexible membrane, said membrane bearing an electrically conductive layer and a probe species layer, and the bottom of said rigid cavity bearing a photo controlled conductive element and electrical contacts attached to an electrical signal source, such that illumination of said conductive element controls an electrical voltage between the bottom or sides of the cavity and the electrically
25 conductive layer of the membrane, and such that the membrane is deflected by an electrostatic force controlled by the electrical voltage; and
an optical addressing system that directs illumination to selected elements of the array at selected modulation frequencies, and
a system to detect the response of the drum-like structures to the selected
30 frequencies and infer any change in an amount of target species hybridized to said probe species.

20. An optical read-out system for a hybridization array sensor of the type having an array of deflectable membrane modulators, the resonant frequency of each membrane modulator controlled by hybridization of a target species to a probe species on the membrane of the membrane modulator, said system

5 comprising

a signal source and driver to drive the entire array of modulators at a series of selected frequencies,

an optical phase detection system to measure phase differences between the signal source and the deflection of the modulators at the selected

10 frequencies, and

an information processing system to relate the phase differences to changes in the hybridization state of the membrane modulator.

21. A system for producing chemical arrays on a roll-to-roll basis

15 comprising:

a plurality of exposure modules each comprising a variable masking system, a light source and imaging optics to image a line of pixels from a variable mask to a line on a surface,

a plurality of photochemical modules to bring reactants of a photo
20 controllable chemistry in contact with a substrate bearing reaction loci, such that at each photochemical module is associated with at least one exposure module such that the variable masking system of the exposure module controls illumination of a line of reaction loci on the substrate and thereby controls the photo-controllable chemistry in a spatial pattern of loci according to the variable
25 masking system, such that the plurality of photochemical modules and their associated exposure modules effect an individually predetermined sequence of photo-controlled reactions at each locus on the substrate.

22. A roll-to-roll DNA array manufacturing system comprising a web
30 handling system to move a substrate in the form of a flexible web through a series of groups of four photochemical reactors, each of said photochemical reactors comprising a source of photo-controlled chemistry and an exposure module such that reactive molecules on the substrate are brought into contact

with each of four nucleic acids A, G, C, T, in a predetermined order and the exposure module controls the illumination of the substrate at each of a plurality of loci in a line on the substrate substantially perpendicular to the direction of web motion and on the substrate in a predetermined spatial pattern.

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23. The method of claim 1, wherein said second substrate comprises an array of vibratory elements formed on said substrate, each element having a vibratory membrane having with a characteristic resonance frequency, when activated by an oscillating electrical field applied to the membrane, and said
10 positioning step includes placing the second substrate into a confronting relationship with the master array, such that biomolecules bound to the master-species array are in proximate confronting relationship to corresponding vibratory elements in the second substrate.

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24. A sensor device comprising
a substrate having a plurality of array regions,
attached to each array region, an anchoring nucleic acid covalently
attached to each region, said anchoring nucleic acid having a common base
sequence, and

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hybridized to the anchoring nucleic acid in each region, a nucleic acid
probe having a first common-sequence region that is complementary to at least
a portion of the anchoring nucleic acid, and a second probe region having a
nucleic acid sequence that is different in the different regions.

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25. The device of claim 24, wherein the anchoring and common-
sequence nucleic acids are covalently coupled to one another.